V 503/29287

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L3 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:15500 CAPLUS
DN 132:220058
TI NELL-1 enhances mineralization in fetal calvarial osteoblastic cells
AU Kim, David; Soo, Chia; Zhang, Xinli; Park, Howard; Wang, Yubert; Longaker, Michael T.; Ting, Kang
CS Departments of Surgery and School of Dentistry, Section of Orthodontics, Los Angeles, Medical Center, University of California, Los Angeles, CA, USA
SO Surgical Forum (1999), 50, 599-601
CODEN: SUFOAX; ISSN: 0071-8041
PB American College of Surgeons
DT Journal
LA English
AB The association of NELL-1 expression with bone formation and mineralization of the calvarial osteoblast-like cells was studied. NELL-1 mRNA was faintly expressed from day 14 of gestation with mild increase over the gestation period. Both primary rat fetal calvarial cell cultures and MC3T3 cell cultures overexpressing NELL-1 showed an increase in mineralization. Mouse cDNA array results from NELL-1-infected MC3T3 cells showed the expression modulation of the genes related to bone formation and craniofacial development: downregulation in BMP-7 gene expression and upregulation of Split Hand and Foot gene.

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L3 ANSWER 7 OF 28 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2001-300143 [31] WPIDS
DNC C2001-092112
TI Screening for an agent that alters bone mineralization, useful for facilitating bone calcification or repair, comprises contacting a cell containing NELL-1 gene with a test agent and detecting a change in NELL-1 gene expression level.
DC B04 D16 D22
IN TING, K
PA (REGC) UNIV CALIFORNIA; (TING-I) TING K
CYC 94
PI WO 2001024821 A1 20010412 (200131)* EN 54
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000079943 A 20010510 (200143)
US 2003158602 A1 20030821 (200356)
ADT WO 2001024821 A1 WO 2000-US27477 20001004; AU 2000079943 A AU 2000-79943 20001004; US 2003158602 A1 US 1999-412297 19991005
FDT AU 2000079943 A Based on WO 2001024821
PRAI US 1999-412297 19991005
AB WO 200124821 A UPAB: 20010607
NOVELTY - Screening (M1) for an agent that alters bone mineralization comprises contacting a cell containing a NELL-1 gene with a test agent, and detecting a change in the expression level of the NELL-1 gene as compared to the expression in a cell that is not contacted with the test agent at a lower concentration.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) pre-screening (M2) for a NELL-1 modulator comprises contacting a NELL-1 nucleic acid or protein with a test agent, and detecting specific binding of the test agent to the NELL-1 nucleic acid or protein;
(2) increasing (M3) bone mineralization comprises increasing the concentration of a NELL-1 gene product in an osteogenic cell;
(3) facilitating (M4) the repair of bone fractures comprises increasing concentration of a NELL-1 gene product at or near the fracture site;
(4) facilitating (M5) the repair of a bone fracture comprises contacting the bone fracture site with a NELL-1 protein;
(5) bone graft material (I) comprising a biocompatible matrix and a NELL-1 protein capable of enhancing the formation of osseous tissue in the animal in which it is implanted; and
(6) bone graft material, which is capable of inducing the formation of osseous tissue in the animal in which it is implanted, comprising a collagen conjugate containing 65-95 weight% reconstituted collagen and 5-35 weight% NELL-1 protein.
ACTIVITY - Osteopathic.
Whole mouse embryo RNA analysis from fetal gestation day 7, 11, 14 and 17 was performed. Adenovirus carrying NELL-1 cDNA was constructed and infected into rat fetal calvarial primary cell cultures and MC3T3 cell lines. Adenoviruses containing the beta -galactosidase gene were used as control and examined for efficacy of infection with different cell types. NELL-1 mRNA was faintly expressed from day 14 of gestation with mild increase over the gestation period. Both primary fetal calvarial and MC3T3 cell cultures over expressing NELL-1 showed an increase in mineralization over the beta -galactosidase control. Over expression of

NELL-1 enhanced mineralization in calvarial osteogenic primary cell cultures by approximately 30 folds on day 17-post infection compared to the control. Results confirmed that NELL-1 is closely associated with bone formation and it enhanced mineralization of the calvarial osteoblast-like cells.

MECHANISM OF ACTION - None given.

USE - (M1) and (M2) are useful for identifying agents that enhance bone mineralization (claimed).

(M3-5) are useful for repairing bone fractures, increasing bone density, or to induce bone repair (claimed).

(I) is useful as bone graft materials for the treatment of fractures (claimed) or to facilitate replacement or healing of prostheses or bone transplants.

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